ACOUSTIC REFLECTOMETRY AND HEARING LOSS IN PEDIATRIC PATIENTS WITH ACUTE OTITIS MEDIA

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This study investigated the ability of acoustic reflectometry to predict conductive hearing losses in patients diagnosed with acute otitis media in a primary care pediatric practice. We examined the potential association between acoustic reflectometry and threshold audiometry in ninety-eight patients between the ages of four and twenty years. Reflectivity was significantly associated with a four frequency pure tone average of hearing recognition thresholds. The correlation coefficient for this association was 0.651 ($p<.001$).

Failed audiograms were defined as those with at least one threshold of 25 dB or greater. Using a reflectivity of 6.0 or higher, we found that we were able to predict failed audiograms with sensitivity of 75.9% and a specificity of 83.3%. The reflectivity cutoff value could be raised or lowered to maximize various indices of diagnostic efficacy.

We obtained follow up reflectometry and audiometry data on fifty infected ears. We used that information to examine the association betwen the *change* in acoustic reflectivity and the *change* in four frequency pure tone average between two visits. That association yielded a correlation coefficient of 0.740 ($p<.001$).

Thus, acoustic reflectometry is useful for predicting the degree of conductive hearing loss in patients with acute otitis media, and also useful for following the progression of such hearing deficits.

Introduction:

Otitis media is a common illness which affects most children, and accounts for a great number of visits to primary care physicians each year. Otitis media is, in fact, the most common infectious disease of childhood after respiratory tract infections (Blood *et al*, 1990).

Otitis media has been defined in several ways, but most commonly is understood to refer to inflammation in the middle ear cavity (Scheidt and Kavanagh, 1986). Acute otitis media usually refers to effusion in one or both middle ears accompanied by one or more signs of acute illness including fever, otalgia, otorrhea, ear tugging, irritability, lethargy, anorexia, vomiting or diarrhea (Teele *et al*, 1989).

Epidemiology:

The epidemiology of acute otitis media emphasizes the common nature of this problem. Data from the Greater Boston Otitis Media Study Group has revealed that by the end of the first year of life, a full sixty-two percent of children have had at least one episode of acute otitis media, while seventeen percent have already experienced at least three episodes. By the time the children in the Greater Boston study group had reached three years of age, 83 percent of the subjects had faced at least one episode, while 46 percent of the children had experienced at least three episodes (Teele *et al,* 1989). In light of these figures, it is not

surprising that according to some estimates, acute otitis media accounts for one-third of all office visits to pediatricians (Blood *et al*, 1990; Schwartz and Schwartz, 1980; Pukander *et al*, 1984). The highest incidence of episodes of acute otitis media was found to be during the second half of the first year of life. Later in life, there is a second lower rise in incidence between the ages of four and five years, presumably associated with increased sick contacts when children begin school (Teele *et al*, 1989).

Season also plays a critical role in the epidemiology of acute otitis media, with the majority of cases occurring during the winter months. The incidence of acute disease drops off rapidly outside of this time period (Pukander *et al*, 1984).

Individual children may have very different experiences with otitis media. Some children are rarely, if ever, stricken with acute inflammation of their middle ear spaces, while other children seem particularly susceptible to recurrent episodes of acute otitis media (Klein *et al*, 1992).

The Greater Boston Study also demonstrated that several factors are associated with increased risk for suffering from recurrent middle ear disease. Male gender, for example seems to be associated with a greater risk for acute otitis media. Recurrent disease in a sibling is also associated with increased risk for middle ear disease. This latter association points out a possible genetic susceptibility to acute otitis media. The actual trait which is responsible for that genetic trend has not been established. The assumed defect may have an anatomic, physiologic or immunologic basis.

The age at which a child is first affected by acute otitis media was found to be one of the strongest predictors of subsequent recurrent middle ear disease. It seems as though the earlier a child is first diagnosed with acute otitis media, the more likely that child will suffer from recurrent disease. In fact, children who do not experience acute otitis media by the age of two years are unlikely to later have problems with recurrent disease (Klein *et al*, 1992).

Interestingly, breast feeding also seems to play a role in the epidemiology of middle ear disease. The Greater Boston study found that breast feeding was strongly associated with a

decreased risk for otitis media during the first year of life. Initial thoughts were that perhaps the upright position of breast feeding prevented nasopharyngeal reflux and the possible resulting eustacian tube interference. Since the duration of the breast feeding does not seem to be a protective factor, however, and because infants fed breast milk by a bottle also experience fewer bouts with otitis media, the mode of feeding is no longer thought to be important. Current thoughts presume an immunologic advantage to breast milk or perhaps an immunologic disadvantage to cow milk or formula. One study in 1984 demonstrated a protective effect of breast milk against otitis media among a group of infants with cleft palate (Paradise and Elster, 1984).

Exposure to day care settings and parental cigarette smoking are also thought to be important by some authors, though the correlation to acute otitis media is less clearly defined (Pukander *et al*, 1984).

Pathogenesis:

The pathogenesis of acute otitis media is usually explained in the following manner. A respiratory infection or environmental event causes congestion of the mucous membranes lining the upper respiratory tract. Thickening of the mucosa of the eustachian tube leads to obstruction of the tube's lumen at its narrowest portion, the isthmus. Secretions from the mucosa of the middle ear now collect distal to the obstruction, in the middle ear space, providing a hospitable environment for the proliferation of bacterial pathogens, which happen to be trapped in the same environment (Klein, 1992).

The most common bacterial pathogens responsible for infecting the fluid collections of the middle ears of children are Streptococcus pneumoniae (29%) and Haemophilus influenzae (20%). Less common, but also important pathogens include Branhamella catarrhalis (6%), Staphylococcus aureus (2%) and group A Streptococcus (2%) (Klein *et al*, 1992). Viruses, especially the respiratory syncytial virus, are assumed to be responsible for some of the remaining episodes of acute otitis media in which bacterial pathogens cannot be found (Klein BS, 1982).

Sequelae:

Considering the pathogenesis of acute otitis media, one of the obvious consequences of this disease is collections of fluid, or effusions, in the middle ear space. Eventually, these effusions resolve as eustachian tube function returns to normal. This process, however, takes a variable amount of time. Appropriate antibiotic therapy typically sterilizes the middle ear effusion in a few days, and symptoms of the acute inflammation usually subside in that period of time. It is very important clinically that the fluid itself may persist for weeks or months after an episode of acute otitis media (Klein, 1992).

Persistence of effusions in the middle ear space was demonstrated in the study of the children from the greater Boston area. The investigators found that 70% of children still had middle ear effusions two weeks following diagnosis of acute otitis media. Forty percent of subjects still had middle ear effusions one month after diagnosis, 20% at two months and 10% of children still had middle ear effusions a full three months after receiving the diagnosis of acute otitis media (Klein *et al*, 1992).

Combining this knowledge of the time course for resolution of middle ear effusions with our understanding of the high incidence of otitis media, one realizes that many individuals spend a considerable amount of their childhood with effusions in their middle ear spaces. This fact is especially concerning when one considers the sequelae of middle ear effusions in childhood. Perhaps the most important result of fluid in the middle ear space is the accompanying hearing loss that children experience (Olmsted *et al*, 1964).

This conductive hearing loss that children with effusions experience is usually not permanent (Olmsted *et al*, 1964). Presumably, it results from the decreased mobility of the tympanic membrane or the ossicular chain, secondary to a collection of fluid resting in the middle ear. Acoustic vibrations which typically are efficiently transmitted across the tympanic membrane to the bones of the middle ear are dampened and reflected from the membrane in the presence of an effusion. Most studies which have examined the hearing acuity of infants and children with middle ear effusions conclude that fluid in the middle ear produces a mild

to moderate hearing loss, approximately 25-30 dB at the frequencies most commonly associated with human speech, 500 to 4000 Hz (Fria *et al*, 1985; Silva *et al*, 1986; Chase, 1992).

Hearing deficits as great as 40 dB are classified as "mild" hearing loss by the American National Standards Institute (Herrmann, 1992). This level of hearing loss can be quite handicapping, however, when we consider that each 10 dB reduction in intensity results in a signal which is perceived to be only one-half as loud (Davis, 1986). The degree of hearing loss associated with middle ear effusions, therefore can have great significance. Indeed, hearing deficits as mild as 14 dB are thought to render some aspects of speech inaudible (Skinner, 1978; Chase, 1992).

Contributing to the significance of these deficits is the fact that some studies have shown that the hearing loss caused by middle ear effusions may take several months to resolve. Many patients (12.2%) still have hearing loss six months after the acute infection (Olmsted *et al*, 1964).

The incidence of otitis media is highest in the preschool years, especially in the first two years of life. Thus, it seems likely that children will be experiencing fluctuating hearing loss and inconsistent auditory signals at the same time that they are developing their language skills (Feagans, 1987).

With these concerns in mind, it seems plausible that children who experience more otitis media, or who spend more time with effusions in their middle ears might suffer from delays in linguistic development. These concerns have resulted in the past several years in great interest in examining the sequelae of the fluctuating, transient mild to moderate hearing loss associated with bouts of otitis media.

The greater Boston otitis media study group, in their seven year prospective study, found that the estimated time spent with middle ear effusions in the first three years of life was significantly associated inversely with intellectual ability, school achievement, speech and language skills at seven years of age (Teele *et al*, 1990). After adjusting for socioeconomic

status and gender, the investigators found that subjects in their study who spent the greatest amount of time with middle ear effusions prior to the age of three scored 8 points lower on a full scale WISC-R IQ test. Similar significant differences were noted for verbal and performance IQ. The study group also found inverse associations between the time spent with middle ear effusions and scores on reading and mathematics achievement tests, as well as on assessments of speech and language abilities at seven years of age (Teele *et al*, 1990).

Other studies have found that early persistent middle ear disease is associated with increased incidence of delays in language development. One such study demonstrated that among a group of otitis-prone infants, over seventy percent of subjects exhibited language delay, with over forty percent delayed by at least six months as judged by two objective scales of language development (Friel-patti *et al*, 1982). Other investigations have found that these delays may persist throughout much of the preschool years (Schlieper *et al*, 1985).

Interestingly, the effects of otitis media and dampened hearing secondary to middle ear effusions seem to reach further than simple language delays. As the greater Boston study group began to demonstrate, and many other authors have begun to hypothesize, recurrent otitis media or persistent middle ear effusions in infancy and early childhood may have a prolonged impact on cognitive development, behavior patterns and learning skills.

Models of cognitive development differ in the manner in which they view the infant and in what, if any, biological endowments they presume for the infant mind. All models, however, seem to agree that widely varied sensory input is a crucial feature to the healthy cognitive development of an individual (Feldman and Gelman, 1986). It follows, therefore, that the reduction and inconsistency in auditory signals received by an infant with fluctuating middle ear effusions could potentially affect that child's cognitive development.

Also, some behaviorists contend that particular patterns of behavior could be different for a child with fluctuating mild to moderate hearing deficits, because of the manner in which they perceive their environment and how individuals in that environment perceive and treat them. Once these altered types of behaviors are learned, they might possibly persist

throughout childhood and well beyond. Several researchers have attempted to assess these potential differences in behavioral and cognitive development.

A study by Zinkus and Gottlieb, in 1980, began to search for differences in the cognitive skills of children with a history of chronic ear problems. In addition to confirming the presence of language and speech delays, they found that these children also were deficient in their auditory processing skills. The group of children with the history of otitis media had difficulties performing tasks which required attention. The authors thus suggested that exposure to early or recurrent otitis media may have led to problems in generalized attention (Zinkus and Gottlieb, 1980).

Some more recent studies have examined the relationship between early middle ear disease and later attention skills. Feagans *et al* suggest that for children with otitis media, listening and understanding take greater effort than for children without otologic problems. They propose that this difference might account for a reduced attention to language which is ultimately responsible for the long-term sequelae of early middle ear disease. These researchers studied young school children to validate their hypotheses. They found that their frequent otitis media group had significant deficiencies in narrative skills and proposed that these deficiencies were the result of the attention deficits that these children also seemed to display. In the classroom, for example, these students with a significant otitis history had twice as many intervals in which they were found off-task (Feagans *et al*, 1987).

Many other researchers have searched for distinct behavioral problems associated with a history remarkable for otitis media. It is plausible that the proposed attentional deficits of these individuals might contribute to some of these behaviors. Investigators in New Zealand, as part of the Dunedin Study, have searched for some of the presumed behavioral problems which are associated with chronic middle ear effusions. In 1986, Silva *et al* reported that their group of children with bilateral ear effusions not only had significantly lower scores on tests of verbal comprehension and expression, but also were reported to have more behavior problems (Silva *et al*, 1986).

Another group of New Zealand researchers sought to define specifically these behavioral problems. They found that the Dunedin Study children with significant histories of middle ear effusions were not only disadvantaged in speech articulation, verbal comprehension and intelligence, but that they also exhibited deficits in motor development. This group of children also displayed several specific behavioral problems. They were judged to be "significantly more dependent, to have shorter attention spans, and to show weaker goal orientation. They were reported by their parents to be more restless, fidgety, destructive, less popular, and more often disobedient" (Silva *et al*, 1982).

It is obvious from the previous discussion that persistent or recurrent problems with otitis media and the accompanying hearing deficits can be associated with a variety of associated deficiencies in cognitive, linguistic and behavioral development. All of these factors, which are presumed sequelae of early middle ear disease seem to set the stage for some children to have significant disadvantages in educational and social environments. Indeed, research has found a disproportionate number of children with a history of otologic pathology among populations of students classified as "learning disabled" (Masters and Marsh, 1978).

A difficulty arises when one attempts to address causality. Researchers have been very careful to point out that these findings are merely associations, and that the actual causes of these potential childhood disadvantages have not been entirely elucidated. While many authors suggest that these differences in developmental skills might be the direct result of the hearing loss associated with fluctuating middle ear effusions, several offer alternative explanations which may, at least in part, be responsible for the differences in groups with significant otitis. Some authors propose that there may be common factors, environmental or genetic, which predispose children to both otitis media and poorer performance on academic or developmental tests (Teele *et al*, 1990). It is also possible that some of these developmental differences might be the result of chronic illness and less directly related to the hearing deficits. Perhaps, for example, those children who are chronically inflicted with middle ear disease experience a disruption to their sense of wellness. They might even

experience some chronic discomfort. Either of these factors may diminish a child's normal drive to learn (Friel-patti *et al*, 1982).

Other authors propose that frequently ill children might be treated differently by others. Differences in interactions with parents, teachers and peers could certainly play a role in establishing alternate developmental and learning patterns (Teele *et al*, 1990).

Still other authors propose more physiologic explanations to account for the findings among children with frequent otitis media. Webster, for example, demonstrated that mice that suffered from experimentally produced conductive hearing loss during a critical period postnatally developed significantly smaller than normal neurons in the auditory tract of the brain stem (Webster, 1984).

Other investigators have also proposed neurologic dysfunction as the mediator of the developmental sequelae of hearing loss from otitis. One such study examined learning disabled children and adolescents with a history of early onset, recurrent otitis media. Their results indicated that, compared to a similar group of subjects without the otologic history, the otitis-prone group suffered from persistent, serious cognitive deficits. These authors proposed a relationship between the hearing deficits associated with middle ear pathology and auditory-cortical dysfunction (Secord *et al*, 1988).

Although the precise physiologic or developmental mechanisms are not clear, studies cited above have indicated that childhood otitis media and the accompanying hearing loss are associated with several significant and potentially damaging sequelae. Considering the seriousness of these sequelae and the high prevalence of this pathologic condition during the first several years of life, the potential implications are great. It has become, therefore, crucial that these effects be investigated further and that they be addressed from a preventive perspective. Physicians caring for children need to develop ways to identify which children are susceptible to recurrent or persistent bouts of otitis media. Sensitive, reliable, cost-effective ways to document and follow the presence of middle effusions and the presence of conductive hearing losses are critical.

Acoustic Reflectometry:

In 1984, Teele and Teele introduced acoustic reflectometry, a new technique to detect middle ear effusions. This new technology was developed by John Teele, who was a radar engineer and intelligence analyst (Klein *et al*, 1992). The device works by directing a pulse of sound at the tympanic membrane and subsequently measuring the amplitude of the resulting sound wave which is the sum of the incident and reflected wave patterns. Figure 1 shows a simplified diagram of the acoustic refectometry device demonstrating the relative positions of the device's speaker and microphone.

As predicted by the physical laws of acoustics, the sound wave reflected from the tympanic membrane will partially cancel the original wave, resulting in less sound ultimately being detected by the microphone on the hand-held transducer. The maximal amount of cancellation between the waves occurs at a point which is one-quarter the wavelength of the incident sound pulse away from the reflective surface (Figure 2).

The acoustic reflectometer identifies the sound frequency which places that quarter-wavelength nadir in sound pressure at the distance of the device's microphone. At that particular frequency, when the reflected sound wave is completely out of phase with the incident sound, the microphone can detect that maximal drop in sound pressure (Teele and Teele, 1984). Considering the properties of sound waves, one can see that the amount of reflected sound is inversely proportional to the total resultant sound; the greater the amount of sound reflected off the tympanic membrane, the less total sound will be detected by a microphone on the transducer (Bess, 1986).

It is these properties which makes the acoustic reflectometer useful for detecting middle ear effusions, and potentially useful for investigating conductive hearing loss. In the presence of an effusion, the acoustic impedance of the middle ear is increased (Bluestone and Klein, 1988). With this increased impedance, the tympanic membrane-middle ear system will not transmit sound as efficiently to the cochlea. In this situation, a greater amount of sound will be reflected off of the tympanic membrane, and less sound will be transmitted through to

the neural apparatus of the inner ear (Bluestone and Klein, 1988).

Thus, the technology of acoustic reflectometry could be useful in detecting the greater amount of reflected sound due to increased middle ear impedance. Because a greater amount of reflected sound implies that less sound has been transmitted to the middle ear, this same technology might be useful for predicting the presence of associated conducting hearing losses (Teele *et al*, 1990).

The current device used for acoustic reflectometry is produced by ENT Medical Devices in Wareham, Massachusetts. It generates a harmless 80 dB sound pulse which sweeps a frequency range from 2000 to 4500 Hz in 100 milliseconds (Bluestone and Klein, 1988). The hand-held sound transducer is placed next to the meatus of the patient's external auditory canal, so the sound pulse is directed toward the tympanic membrane. A microphone on the tip of the transducer measures the total level of transmitted and reflected sound. The device then generates its output of reflectivity, a value on a scale from 0.0 to 10.0. A higher value indicates more cancellation of sound, and therefore, more sound reflected off of the tympanic membrane, presumably indicating a greater impedance of the middle ear apparatus.

The inventors of acoustic reflectometry have proposed that this technique has several significant advantages over the other available objective technology for detecting middle ear effusions, tympanometry. This latter technique requires a considerable amount of cooperation from the child being tested. Tympanometry requires a hermetic seal in the ear canal. This seal can be quite difficult to establish and maintain in an uncooperative child. Tympanometry also uses a pulse of pressure which can be quite uncomfortable, especially in an acutely infected, tender ear. In addition, some investigators believe tympanometry is inaccurate in infants (Teele and Teele, 1984).

Since the acoustic reflectometer relies on a pulse of sound rather than pressure, it requires no seal in the ear canal. The level of sound utilized by the device is thoroughly harmless and renders the technique completely free from discomfort. Furthermore, acoustic reflectometry is completely portable. Its results are achieved virtually instantaneously. It was also designed

to give results which are independent of age, crying or the presence of cerumen partially obstructing the ear canal (Teele and Teele, 1984).

The inventors of acoustic reflectometry conducted a study to establish the accuracy of their newly introduced technology to predict the presence of effusions. They used pneumatic otoscopy and tympanometry to confirm the presence or absence of a middle ear effusion. Using a cut-point of 4.0 reflectivity units, they found a sensitivity of 94.4% and a specificity of 79.2% for the acoustic reflectometer to detect an effusion in pediatric aged patients. The authors chose that cut-point to maximize both positive and negative accuracy. They suggest that, depending on the intended use of the technique, the cut-point could be lowered to maximize sensitivity or could be raised to maximize specificity (Teele and Teele, 1984).

Several other investigators have examined the association between the presence of middle ear effusions and abnormal reflectivity of the tympanic membrane by acoustic reflectometry. Using a cut-point of 5.0 reflectivity units, one study by Jehle and Cottington found a sensitivity of 82.1%, a specificity of 100%, with a positive predictive value of 100% (Jehle and Cottington, 1989). Other studies have had varied results, with sensitivities ranging from 54 to 94 percent and specificities from 59 to 100 percent (Macknin *et al*, 1987; Klein *et al*, 1992). Most studies have concluded, however, that acoustic reflectometry provides an objective, reliable, practical adjunct for the diagnosis of middle ear effusions (Jehle and Cottington, 1989).

One of the most common objections to acoustic reflectometry is the complaint by casual users of the device's imprecision (Macknin *et al*, 1987). One author, however, has demonstrated that with a graphic recorder, which reports reflectivity to tenths of units, and in the hands of an observer with some experience, precision does not present a problem. Combs, in a 1988 study, found that upon obtaining ten reflectivity readings for each patient, mean standard deviation of these values was only 0.2 units (Combs, 1988).

The usefulness of acoustic reflectometry to aid in the diagnosis of otitis media with middle ear effusions has been established. The original authors who introduced this technology had

envisaged other applications as well. At the time of this new device's creation, the association between middle ear pathology and hearing loss was established, and several authors were beginning to study the long-term sequelae of conductive hearing loss.

Teele and Teele, who devised and constructed the prototype acoustic reflectometer were interested in ultimately applying their new technology to evaluate the degree of conductive hearing loss in pediatric patients with otitis media. From a theoretical perspective, the device's potential usefulness for this purpose is easy to comprehend. For the patient with a middle ear effusion secondary to otitis media, the acoustic impedance of the middle ear is increased by the presence of fluid behind the tympanic membrane. As discussed above, less of the acoustic energy which enters the external auditory meatus and travels through the auditory canal will be transmitted through the middle ear apparatus to the cochlea.

It is this reduction in transmitted sound energy, and the resultant increase in reflected sound energy which allows the acoustic reflectometer to detect the middle ear effusion. It is that same reduction in transmitted energy which is responsible for the conductive hearing loss associated with otitis media. Teele and Teele proposed that their new technique might indeed be helpful for evaluating conductive hearing loss in patients for whom audiometric evaluation is typically difficult. Their technique would be especially helpful in prelinguistic patients, or those too young to cooperate with and attend to threshold audiometry or play audiometry (Teele and Teele, 1984).

Only one study to date has examined the proposed application of using acoustic reflectometry to evaluate the conductive hearing loss associated with middle ear effusions. That study was done by Teele *et al* on a group of New Zealand children referred for audiologic evaluation. The researchers found that reflectometry was significantly associated with conductive hearing loss. Their study revealed a correlation coefficient of 0.55 between acoustic reflectivity and the average of recognition thresholds at three frequencies. Using a reflectivity of 6.0 to detect a hearing deficit of at least 30 dB, the results demonstrated a sensitivity of 88% and a specificity of 44% (Teele *et al*, 1990).

As stated above, the population studied by Teele et al in New Zealand was comprised of patients referred for audiologic evaluation. This group of patients was more likely to have chronic problems with otitis media and more likely to suffer from hearing losses of various etiologies than the average population of patients seen in a primary care pediatric practice.

In the following study, we attempted to expand upon the existing data by applying this technology in the primary care setting to a group of otherwise healthy children with acute otitis media. In this setting, we believe our findings will be more highly indicative of the potential practical uses of the acoustic reflectometry device which is currently available.

We also sought follow up data from our subjects after a standard course of antibiotic therapy. With this additional information, we hoped to establish that the effusions we were detecting were indeed the etiology of the hearing losses we documented. With follow up data, this study could also examine whether acoustic reflectometry is useful to evaluate clearing of middle ear effusions and whether it can help predict return to normalcy of hearing as well.

Therefore, the following study was designed to address three distinct questions about the value of acoustic reflectometry in acute otitis media.

I. Is there a statistically significant correlation between acoustic reflectivity and conductive hearing loss in patients with acute otitis media?

II. Can cutoff values of reflectivity be defined that would predict failed audiograms with good indices of diagnostic efficacy?

III. Can acoustic reflectometry be used to follow the resolution of conductive hearing losses, thus demonstrating that these losses are transient in acute otitis media and directly related to the middle ear effusions?

The investigators hypothesized that the answer to each of these questions would be affirmative.

If reliable, the association between acoustic reflectometry and conductive hearing losses will be very useful in light of the fact that this technique is quicker and easier to perform than

audiometry, and is feasible in younger, noncooperative patients. The association becomes even more meaningful when we consider the significant sequelae of middle ear effusions that are just beginning to be appreciated. We hope to demonstrate that acoustic reflectometry is a convenient, indirect way to predict and follow significant conductive hearing loss in pediatric patients with acute otitis media.

Methods:

Subjects were recruited at a primary care pediatric practice in New Britain, Connecticut from September, 1992 to January, 1993. Each patient was diagnosed as having either unilateral or bilateral acute otitis media by one of the six primary care pediatricians in the New Britain practice.

Inclusion criteria included the presence of acute otitis media at initiation into the study. To be included, patients also needed to fall between the ages of four years and twenty years. This age range was chosen because normal acoustic reflectivity of the tympanic membrane does not change significantly during this period (Combs, 1990). Younger patients were not invited to join the study also because they cannot reliably cooperate with threshold audiometry techniques.

Exclusion criteria for this study included an age younger than four years or older than twenty years. We also excluded any patient who the primary physician thought to be too unreliable or uncooperative to give accurate audiometric data. Patients with PE tympanostomy tubes in place were excluded from the study as were patients with known or suspected baseline hearing loss.

The primary pediatricians were responsible for making the diagnosis of acute otitis media. This diagnosis was made on clinical grounds. An episode of acute otitis media was defined as effusion in one or both middle ears, detected by plain otoscopy, accompanied by one or more signs of acute illness of recent onset. Accepted signs of acute illness included otalgia, otorrhea and fever. A full, bulging, opaque or erythematous tympanic membrane was

considered further evidence of middle ear involvement, though these finding were variable and not required for diagnosis.

Once the diagnosis of acute otitis media was made, the patients were referred to the principal investigator who then obtained acoustic reflectometry readings and threshold audiometry data for both of the patients' ears. When the subject was diagnosed with a unilateral infection, data were also obtained on the contralateral healthy ear. These healthy ears were included in the total dataset as comparison ears.

Acoustic reflectometry was performed using the Acoustic Otoscope with a 201 recorder from ENT Medical Devices in Wareham, Massachusetts. The most abnormal reflectivity tracing from an approximate five second trial was automatically recorded for each ear in the study. The standard white 10mm disposable tip provided by the company was utilized for each patient. The device was calibrated using its standard, automated calibration procedure each morning before use. Calibration was assured by checking the reflectivity of a standardized calibration tube provided by the manufacturer. The recorder used in this study provided a graphic representation of sound cancellation within the ear canal, and also provided a printout of the acoustic reflectivity value to the nearest tenth of a unit.

Threshold audiometry was performed using the Qualitone Auditory Screener, calibrated professionally at the beginning of the study. The investigators obtained thresholds bilaterally for air conduction at 500, 1000, 2000 and 4000 Hz. Thresholds were obtained to the nearest five dB. A pure tone average hearing level was determined by averaging the thresholds at all four frequencies. Young subjects who were not cooperative or were unable to consistently participate in the audiometric evaluation were dropped from the study.

For the purpose of statistical analysis, a failed audiogram was strictly defined according to American Speech-Language-Hearing Association (ASHA) guidelines. An ear was considered to fail threshold audiometry if any one or more of the four frequencies had a recognition threshold of 25 dB or greater (Bess, 1992).

Threshold audiometry data was collected in a certified sound-proof room which was

specially designed for collecting audiometric data. For maximal consistency, the principal investigator obtained all of the acoustic reflectometry tracings and all of the threshold audiometry data. The principal investigator was trained in the use of threshold audiometry and acoustic reflectometry by a physician familiar with both techniques. The principal investigator then practiced collecting both types of data on several volunteers until he was able to obtain consistent data on multiple trials.

All patients who entered the study were given a ten-day course of antibiotics by the primary physician. The six pediatricians who referred patients to the investigators chose several different antibiotics, including amoxicillin, trimethoprim-sulfamethoxazole, amoxicillin-potassium clavulanate, cefaclor, cefixime and cefuroxime. All patients were asked to return to the office after completing their ten day course of antibiotics.

At the time of follow up, the investigators sought to obtain a second set of audiometry and reflectometry data in order to follow the progression of the middle ear effusions and the accompanying changes in hearing. This second set of data would also allow our study to demonstrate that our subjects' hearing deficits were not baseline deficits, but instead were transient and were directly related to their middle ear disease. Patients who failed an initial course of antibiotics and had persisitent symptoms on follow up were given a second course of antibiotics and asked to return for an additional follow up visit and collection of additional data.

The purposes of the study and the technique of acoustic reflectometry were thoroughly explained to the patients and their families. Verbal informed consent, as approved by the Yale University Human Investigations Committee, was obtained for participation in the study. Subjects were not charged for the any of the tests obtained in pursuit of this research.

Statistical Considerations:

The first question addressed by our study was whether acoustic reflectivity is significantly associated with conductive hearing loss. We assessed this potential association by employing

a correlation analysis using Minitab statistical computer software. Utilizing the four-frequency pure tone average derived from the audiograms as a measure of conductive hearing loss, we conducted a correlation analysis between the ordinal value of acoustic reflectivity and the pure tone average. Regression analyses then enabled the investigators to determine the mathematical relationship between the variables. For all analyses, acoustic reflectivity was considered to be the independent predictor variable, while pure tone average was considered the dependent variable.

The second question posed by the investigators was whether particular cutoff values of reflectivity could be used to reliably predict a failed audiogram. To answer this question, we first needed to define the specific criteria for a failed hearing test. After defining a failed test as one with at least one frequency recognition threshold of 25 dB or greater, we were able to construct two-by-two contingency tables for various reflectivity cutoff points. These tables helped us to evaluate which cutoff value was most useful for predicting a failed audiogram. From our two-by-two tables, we easily determined the sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) for each cutoff. Chi-squared analysis was employed for these tables to investigate statistical significance. To visually represent the usefulness of acoustic otoscopy as a screening device for hearing loss, we constructed a receiver operator characteristics (ROC) curve with several reflectivity cutoff points.

The third question posed by the investigators asked whether acoustic reflectometry could be used to document resolution of conductive hearing losses in patients with acute otitis media, thus demonstrating that these losses are transient and directly related to the accompanying effusions. To answer this question, using data collected on patients at follow up, we calculated the changes in acoustic reflectivity and the changes in pure tone average between two visits. We then employed an additional correlation analysis using the Minitab software, this time examining the *change* in reflectivity versus the *change* in pure tone average.

Results:

Data were collected on ninety-eight patients, ranging in age from four years and one month to twenty years and nine months. The average age of the subjects was just over eight years and seven months (SD 3.8 years). Forty-eight of the patients (49%) were male, while the other fifty patients (51%) were female.

The ninety-eight patients presented with 103 episodes of acute middle ear infections, with five patients presenting with two distinct episodes during the study. Of the 103 infections, twenty-eight of them (27%) were bilateral infections. The other seventy-five episodes (73%) were diagnosed as unilateral. We therefore entered 131 different infected ears into our study. Since unilateral infections provided contralateral healthy comparison ears as well, we also entered 75 healthy ears into the study. This makes the total number of distinct ears entered into the study at initial visit equal to 206.

There were a total of forty-six follow up visits in the study, by forty patients with fifty infected ears. These forty-six follow up visits, along with the 103 initial presentations, brings the total number of patient visits to 149. Since we always obtained data on both ears at each of these 149 visits, the total number of points in the dataset is 298.

Along with the 131 acutely infected ears at initial presentation, twelve ears were diagnosed as still acutely infected at follow up, after a failed course of antibiotics. This brings the total number of observations of acutely infected ears to 143.

Since the forty-six follow up visits yielded data on ninety-two ears, and twelve were deemed infected, eighty ears at follow up were healthy. Along with the seventy-five ears healthy at initial presentation, there were a total of 155 observations made on healthy ears.

The investigator obtaining reflectivity data throughout the study periodically assessed the precision of his technique by finding the standard deviation of multiple trials on the same ear. The standard deviation was always 0.2 reflectivity units or better, based on n=10. This degree of deviation is thought to be evidence of good technique (Combs, 1988).

Study Question I: Is there a statistically significant correlation betwen acoustic reflectivity and conductive hearing loss in patients with acute otitis media?

Acoustic reflectivity was found to be closely associated with the pure tone average derived from the audiograms. The correlation coefficient, r, for this association was 0.651 ($p<.001$). Multiple stepwise regression using acoustic reflectivity (AR) as the predictor variable and pure tone average (PTA) as the dependent variable yielded the following regression equation:

$$PTA=-0.99 + 3.41\ AR\ (t\text{-ratio}=14.7,\ p=0.00,\ R^2=0.424).$$

The total dataset for both infected and healthy ears is presented visually in the scatterplot labeled Figure 3. Additionally, and not shown in Figure 3, the association between acoustic reflectivity and pure tone average remained significant ($r=0.611$, $p<.001$) when we analyzed the subset of ears which were diagnosed as acutely infected.

Study Question 2: Can cutoff values of reflectivity be defined that would predict failed audiograms with good indices of diagnostic efficacy?

143 data points in the study were associated with acutely infected ears, either at initial presentation or after a failed course of antibiotics. The mean acoustic reflectometry reading of these acutely infected ears was 6.5, while the healthy ears averaged 3.8. Our data for reflectivity of healthy ears fits well with previously published norms (Blood *et al*, 1990; Combs, 1990). The two subsets of ears, infected and healthy, differ not only on the basis of their reflectivity results, but they differ also in their pure tone averages. Of the 143 observations made on acutely infected ears, ninety-five, or 66.4% demonstrated failed threshold audiometry. The mean pure tone average for the acutely infected ears was 23.3 dB. This represents markedly worse hearing than the 9.8 dB average for the healthy set of ears. These data are presented in Table 1.

Figures 4 and 5 illustrate visually how the subset of acutely infected ears yielded acoustic reflectometry values which are skewed toward the upper end of the reflectivity scale. Figure 4 shows the values for all ears in the study, healthy and infected. Figure 5 shows similar data

for the infected ears only. Among these infected ears, 79.7% had reflectivity readings of 5.0 or greater, while 53.1% had readings of at least 7.0.

Figure 6 represents the audiometric results of that same subset of acutely infected ears. It demonstrates that at the time of diagnosis, 53.8% of the acutely diagnosed ears were experiencing pure tone averages of at least 20 dB, while 32.9% were experiencing at least 30 dB hearing loss.

A total of 112 ears failed audiometry in our study by the above criteria of at least one frequency having a recognition threshold of 25 dB or greater. Ninety-nine of these (88%) were ears diagnosed as acutely infected. The remaining thirteen ears (12%) were ears not diagnosed as acutely infected, but were the ears contralateral to an infection. The mean pure tone average among the failed audiograms was 28.4 dB (SD 10.2 dB), with a mean reflectivity in these ears of 6.7 (SD 1.8).

We found that, among all ears in the study, the higher the reflectivity of the middle ear, the larger the percentage of subjects who fail their audiometric testing (Figure 7). For any ear presenting with a reflectivity value of 6.0 or greater, there was a 73% chance that ear would fail threshold audiometry by the above criteria. If the reflectivity of that ear, on the other hand, was less than 5.0, there was only an 11% chance of failing audiometry. Ears reflecting between 5 and 6 units were somewhat equivocal (29% failure), not fitting neatly into either category.

Several different arbitrary cutoff values for reflectivity were studied to determine how these different values would serve as screening measures to predict failed audiograms. Sensitivity, specificity, as well as positive and negative predictive values (indices of diagnostic efficacy) for each potential reflectivity screening criterium were then calculated. Lower cutoff points maximized sensitivity and negative predictive value, while higher cutoff points maximized specificity and positive predictive value (Table 2). A cutoff of 5.0, for example, yielded a sensitivity of 85.7% and a specificity of 68.8% for predicting a failed audiogram. If we choose a value of 6.0, the sensitivity drops to 75.9%, while the specificity

improves to 83.3%. Chi-squared analysis demonstrated statistical significance ($p<.001$) in two-by-two contingency tables constructed for each potential cutoff.

The receiver operator characteristics (ROC) curve outlined in Figure 8 provides an additional way of studying these data. The ROC curve examines the relationship between changes in sensitivity of a screening test as a function of changes in 1-specificity. This latter term, 1-specificity, describes the proportion of the screened population who are disease negative, but are said to be positive by the test (false positives). An ideal screening test would have 100% sensitivity with no false positives. A poor test would have low sensitivity with a high rate of disease negative patients falsely identified as being disease positive. Hence, ROC curves which are shifted up and to the left are indicative of better screening tests than those with curves shifted down and to the right.

The ROC curve in Figure 8 is shifted up and to the left. The value of sensitivity remains high over several different levels of 1-specificity. Meanwhile, the value of 1-specificity remains low over a wide range of sensitivities. This shape of the ROC curve indicates that acoustic reflectivity is a useful test for predicting failed audiometry (Bess, 1986).

Judging from ROC curves, the cutoff points with the greatest diagnostic efficacy are those with the highest sensitivity and lowest rate of false positives, in this case a reflectivity of 6.0 (Bess, 1986). This ROC curve, along with the data in Table 2, helps to demonstrate that if a cutoff of 5.0 is chosen, 14.3% of children with failed audiograms will be missed by the screen, while the positive predictive value of the test would be 62.3%. Raising the cutoff to 6.0 improves the positive predictive value of the screening test to 73.3%, but now 24.1% of hearing impaired children would escape detection.

<u>Study Question 3</u>: Can acoustic reflectometry be used to follow the resolution of conductive hearing losses, thus demonstrating that these losses are transient in acute otitis media and directly related to the middle ear effusions?

Seventy percent of the ears which initially failed audiometry passed on their first follow

up visit. If the follow up reflectivity was improved (lower) by 0.5 reflective units or greater, there was a 94.4% chance of an improvement (reduction) in pure tone average by at least 5 dB (n=36). If the reflectivity improved by a full 1.0 units, then there was a 97% chance of that same 5 dB improvement in hearing (n=33). The mean improvement in hearing for those ears with at least a 1.0 unit reduction in reflectivity was 14 dB (n=33).

Among the acutely infected ears for which follow up data were obtained, the *change* in reflectivity was significantly associated with the *change* in pure tone average. This association yielded a correlation coefficient, r, of 0.740 (p<.001). These data are represented graphically in a scatterplot in Figure 9. (Note that changes in reflectivity and hearing may be positive or negative values, depending on whether the follow up observations were improved or worsened.) These data demonstrate, as the investigators hypothesized, the transience of the conductive hearing losses of acute otitis media and, further, that changes in reflectivity can be used to follow the associated changes in hearing losses.

Discussion:

This study demonstrated that acoustic reflectivity is significantly associated with degree of conductive hearing loss during an acute episode of acute otitis media. This is a potentially useful association since acoustic reflectometry is easier and quicker to perform than threshold audiometry. Although our study utilized subjects who were at least four years of age, it is reasonable to postulate that our findings are also applicable to younger children and infants in whom audiometric results are much more difficult to obtain. This assumption makes acoustic otoscopy even more valuable, since it allows the hearing status of prelinguistic children to be estimated quickly and easily in an office setting.

Our study demonstrated that various cutoff values for reflectivity had different indices of diagnostic efficacy for predicting a failed audiogram. Choosing a cutoff of 6.0 seems reasonable to maximize the screening characteristics of the test. Other cutoff values could certainly be chosen depending on the intended use of the test. The cutoff value could be

lowered, for example, in order to maximize the test's sensitivity, while sacrificing positive predictive value. Alternatively, the cutoff could be raised to maximize positive predictive value, while unfortunately, the false negative rate increases and more hearing impaired children are missed.

The preceding point is well demonstrated if one examines the consequences of choosing different reflectivity cutoffs in our study. Using a cutoff of 5.0 would have allowed the investigators to correctly identify 96 (85.7%) of the 112 ears with failed audiograms. The other 16 hearing impaired ears (14.3%) would be falsely assumed to have normal hearing abilities. In correctly identifying the 96 ears, unfortunately, an additional 58 with normal hearing would be incorrectly identified. Those 58 ears represent 31.2% of the 186 ears with normal hearing in this study.

Raising the cutoff to 6.0 would have allowed the investigators to identify only 85 (75.9%) of the 112 ears with significant hearing losses, with 27 impaired ears (24.1%) escaping detection. Using this cutoff, however, only 31 ears with normal hearing would be incorrectly assumed to be impaired. Those 31 ears represent only 16.7% of the 186 ears with normal hearing. This approach, though obviously not perfect, is an improvement over current strategies for follow up of acute otitis media, where no assessment of hearing is routinely done.

Most patients who returned for follow up testing demonstrated measurable improvements in both reflectivity and hearing. This fact demonstrates the transient, reversible nature of the conductive hearing loss associated with acute otitis media. This very rapid improvement was somewhat surprising, however, in light of the fact that the average time spent with middle ear effusions after diagnosis of acute otitis media is greater than 23 days (Teele *et al*, 1989).

Our subjects were asked to return immediately following a ten-day course of antibiotics (mean number of days at follow up = 12). We interpret their partial improvements to mean that acoustic reflectometry is also useful to *follow* the resolution of both middle ear effusions and the accompanying hearing impairment, even though these changes may be subtle. In

fact, we found a statistically significant correlation between the change in reflectivity and the change in four-frequency pure tone average from two visits. This correlation held true regardless of the direction of that change.

We have demonstrated how acoustic reflectometry can be useful for detecting and following the hearing loss associated with acute otitis media. During the course of this research, several clinical situations were noted in which this technology had a particularly useful diagnostic value. Examples from two common scenarios are presented here.

Case 1: J.E. was a six year old boy who was diagnosed with a unilateral left otitis media. Acoustic otoscopy demonstrated a reflectivity of 7.8 in that left ear, which correlated to a four-frequency pure tone average of 40 dB. The patient failed his first course of antibiotics, returning for follow up with continued ear complaints, and an abnormal appearing tympanic membrane. Threshold audiometry and acoustic reflectometry at this time were persisitently abnormal.

After a second course of antibiotics, the patient returned free of complaints, with tympanic membranes which appeared normal by plain otoscopy. The patient's hearing would have been presumed normal if not for our objective measures. The left ear still had a reflectivity of 7.8 with an associated pure tone average of 35 dB. In light of the significant potential sequelae of fluctuating hearing loss in childhood, it is crucial to be aware of and to follow any such deficits. Acoustic reflectometry provides a practical, simple method to do that in an office setting.

Case 2: S.S. was an 8 year old boy who was diagnosed with unilateral acute otitis media on his right side. After two courses of antibiotics, the patient's tympanic membranes looked normal and the patient demonstrated no signs of acute illness. The patient did, however, still complain of unilateral hearing loss. Acoustic reflectometry demonstrated thoroughly normal reflectivity of the right tympanic membrane, making a persistent effusion to account for the loss highly unlikely. The patient was referred to an otolaryngologist for further evaluation of the hearing deficit. In this instance, acoustic otoscopy was important to rule out a persistent

middle ear effusion before making a referral.

Acoustic reflectometry, thus, has practical uses which could play a valuable role in the primary care of children. Currently, acute otitis media is most commonly diagnosed and followed with the aid of otoscopy. Acoustic reflectometry offers several critical advantages over this currently accepted diagnostic technique. As discussed previously, the hearing losses of acute otitis media may have significant long-term sequelae. It is therefore crucial to be aware of these conductive hearing deficits and to follow them to assure their resolution. As illustrated in the first case example above, plain otoscopy will often not detect the effusions which cause hearing loss. The objective technique of acoustic reflectometry, meanwhile, provides a practical, reliable way to follow changes in the conductive hearing losses of acute otitis media.

The changes in reflectivity between initial and follow up visits are often small, yet these small changes are associated with measurable changes in hearing. The objective appreciation of such subtle changes is not possible with current standard otoscopy.

Furthermore, it may be difficult to obtain a satisfactory view of the tympanic membrane using otoscopy in the presence of a noncooperative or crying young patient or an ear canal partially obstructed by cerumen. Acoustic reflectometry avoids these obstacles with almost instantaneous objective results with no discomfort to the apprehensive patient.

Further research needs to be done to assure the usefulness of acoustic reflectometry in an infant population. The technology is currently in a state of rapid evolution, and we anticipate that future advances will possibly make the device even more reliable, especially in younger patients.

For many practitioners in the past few years, acoustic reflectometry has provided a reliable, objective adjunct for the diagnosis of acute otitis media. It has been particularly useful in young patients who are not fully cooperative with otoscopy. We have demonstrated that this technique also makes a useful estimation of the degree of conductive hearing loss which accompanies the middle ear effusions of otitis. Our study further demonstrated that

this technology can be used to reliably predict the resolution of these audiometric deficits.

Acoustic reflectometry, therefore, offers an additional critical element in what should be a multi-faceted approach to the prevention, diagnosis, follow up and treatment of acute otitis media. As health care providers, we should strive to find an approach which minimizes the potentially devastating effects of recurrent disease. This approach should include identification of children at risk, interventions to prevent recurrent episodes, development of accurate diagnostic procedures and efficient therapy. This optimal approach will need to include personnel from different areas of health care, including pediatricians, otolaryngologists, audiologists, and speech pathologists. In light of the significant developmental deficits that have been associated with otitis media, the new approach we develop to treat these children will need to be employed not just in the physician's office, but in the classroom and home as well.

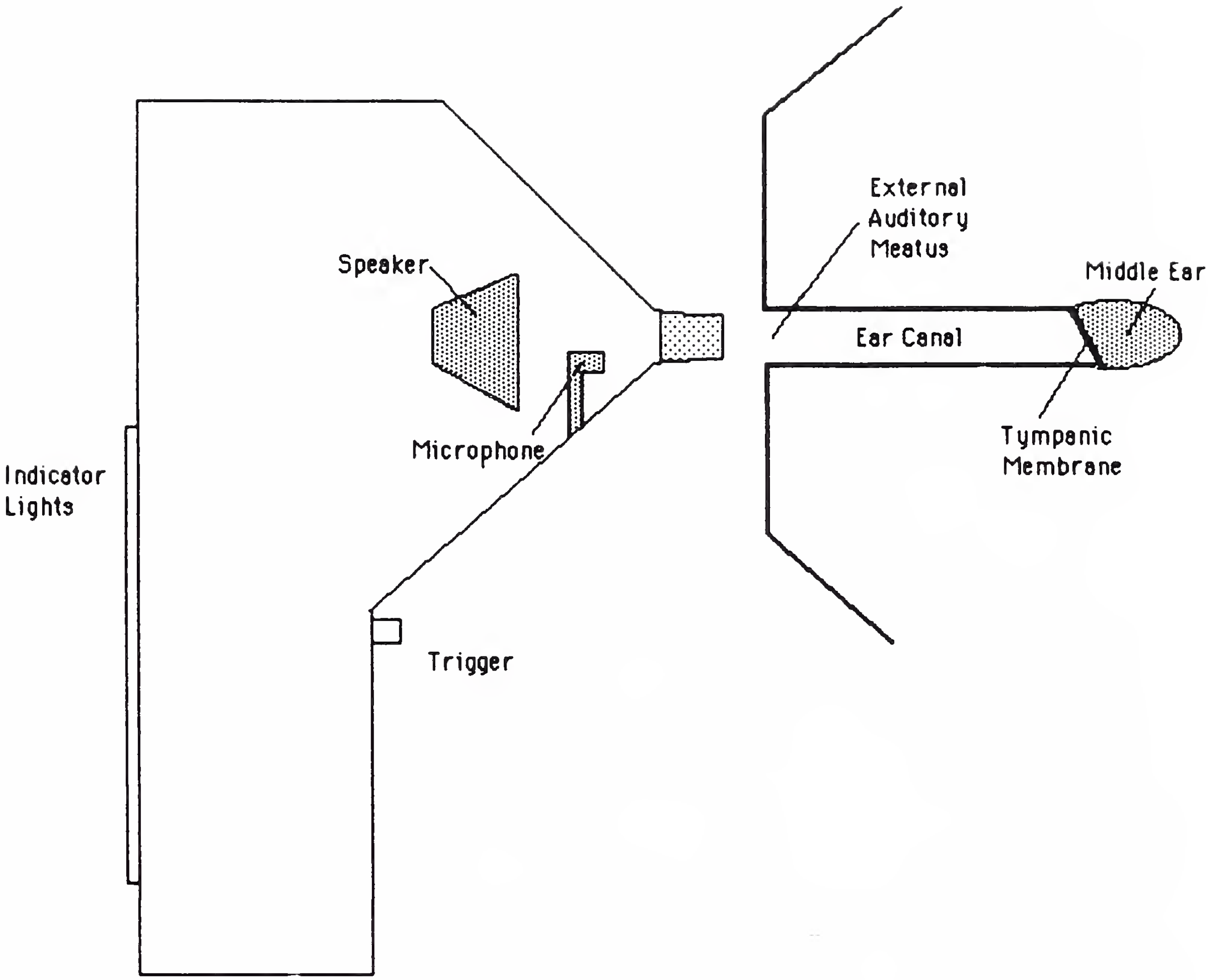

Fig. 1: Simplified diagram of the acoustic reflectometer.

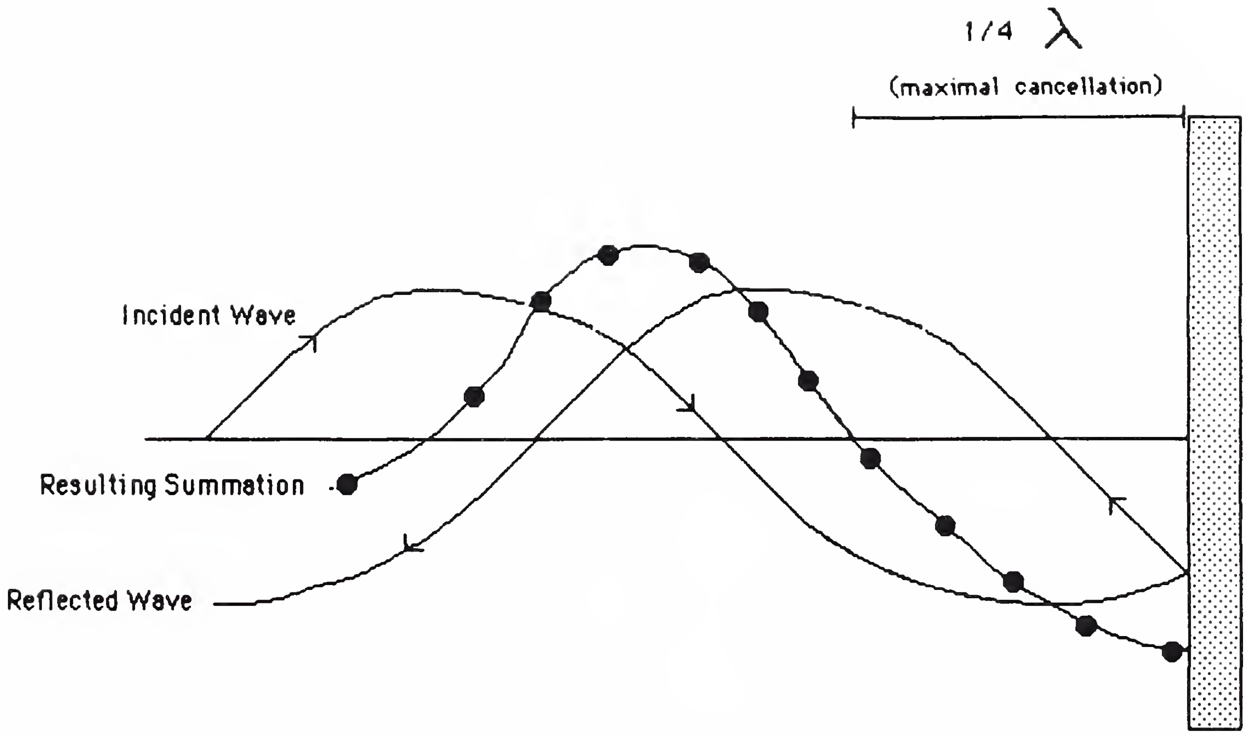

Fig. 2: Behavior of sound waves in a closed-ended tube. Incident and reflected waves interact, with maximal cancellation occuring at a distance of one-fourth of the wavelength away from the reflective surface.

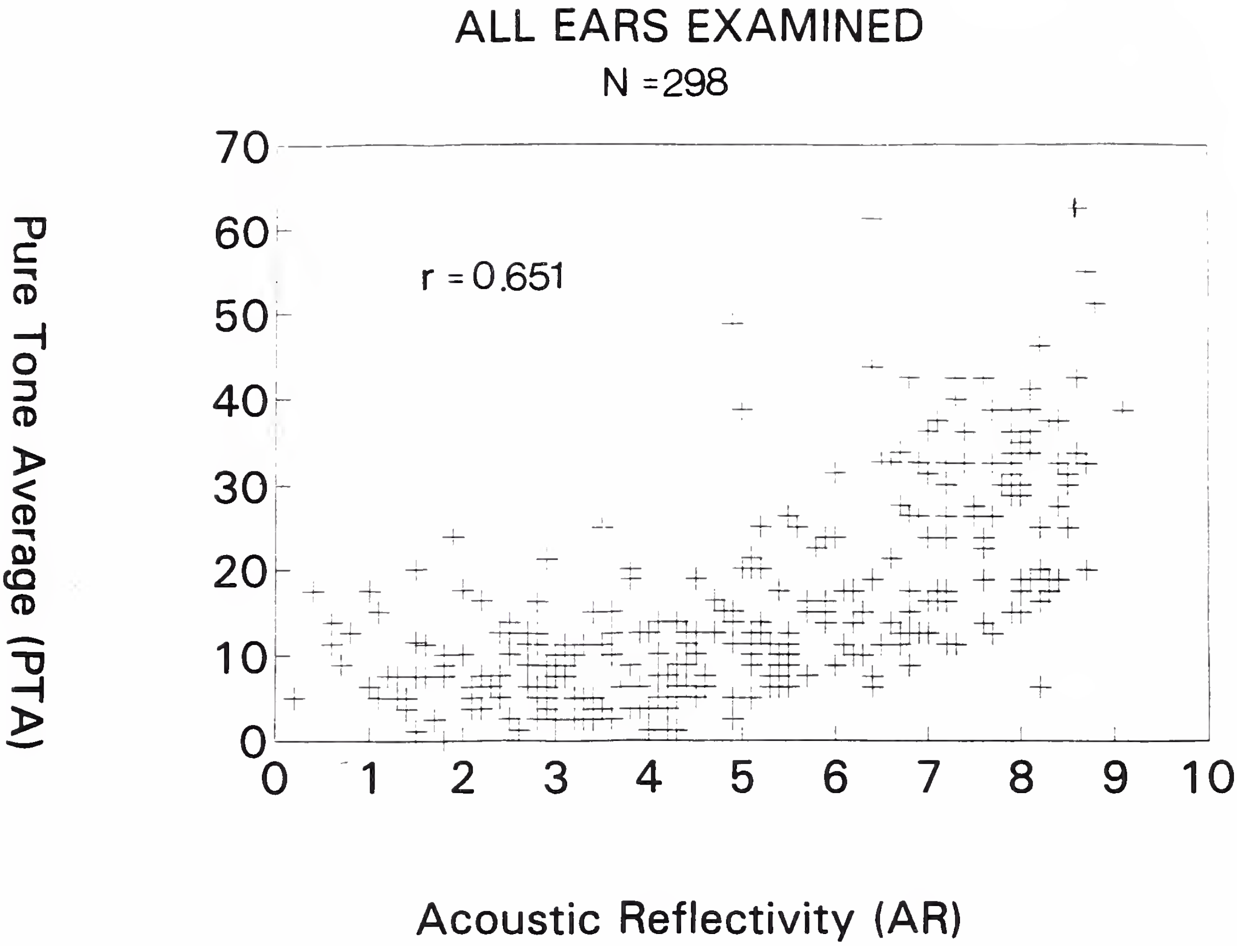

Fig. 3: Scatterplot of data from all ears examined, infected and healthy.

DIFFERENCES BETWEEN ACUTELY INFECTED EARS AND HEALTHY EARS

	TOTAL DATASET	ACUTELY INFECTED	HEALTHY
1EAN AR Stnd. Dev.)	5.1 (2.2)	6.5 (1.8)	3.8 (1.8)
1EAN PTA Stnd. Dev.)	16.3 dB (11.8)	23.3 dB (11.8)	9.8 dB (7.3)

Table 1: Table showing differences in mean acoustic reflectivity (AR) and mean four-frequency pure tone average (PTA) for total dataset (n=298), acutely infected ears (n=143), and healthy ears (n=155).

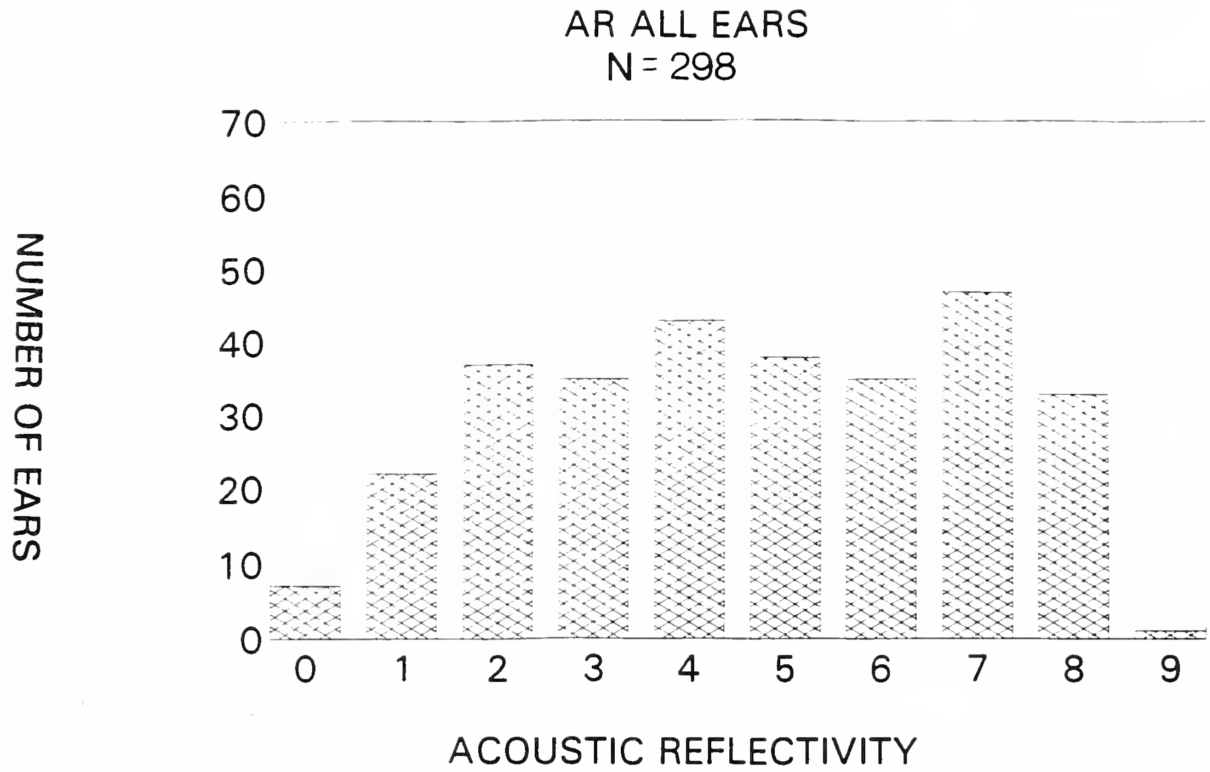

Fig. 4: Distribution of acoustic reflectivity of all ears examined, infected and healthy.

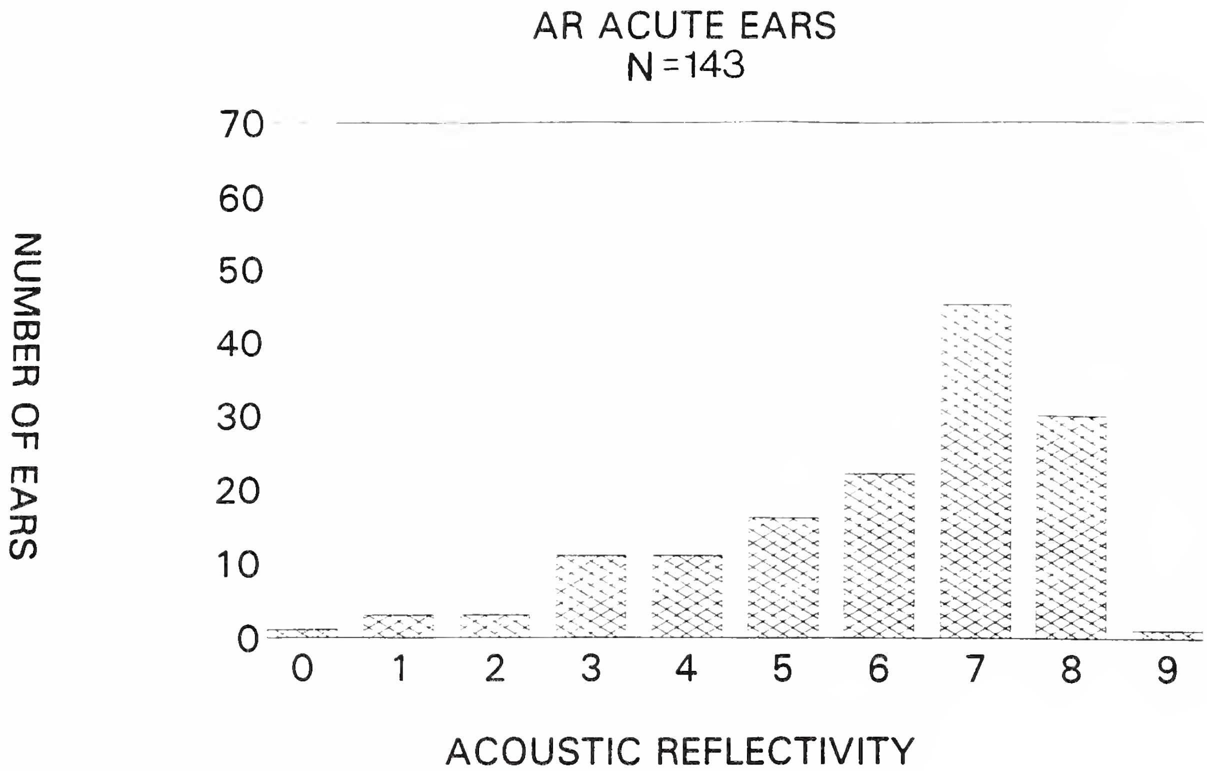

Fig. 5: Distribution of acoustic reflectivity of acutely infected ears.

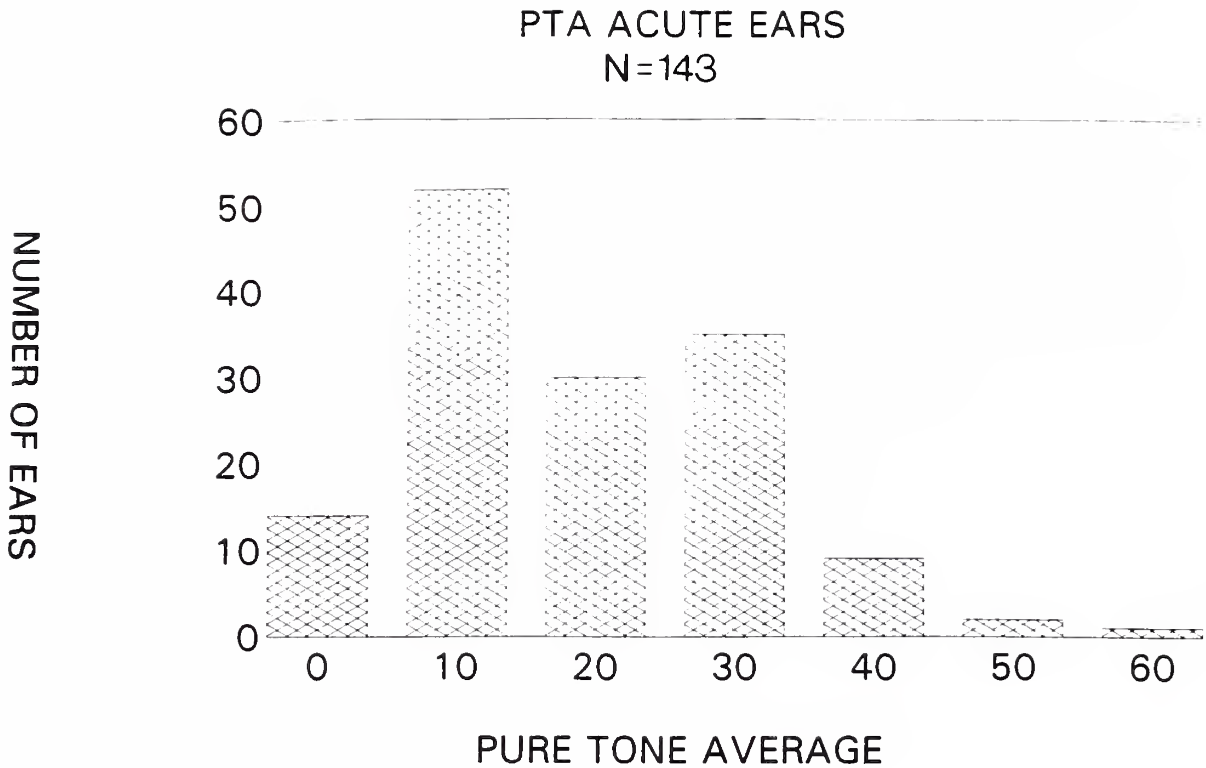

Fig. 6: Distribution of the pure tone average of acutely infected ears.

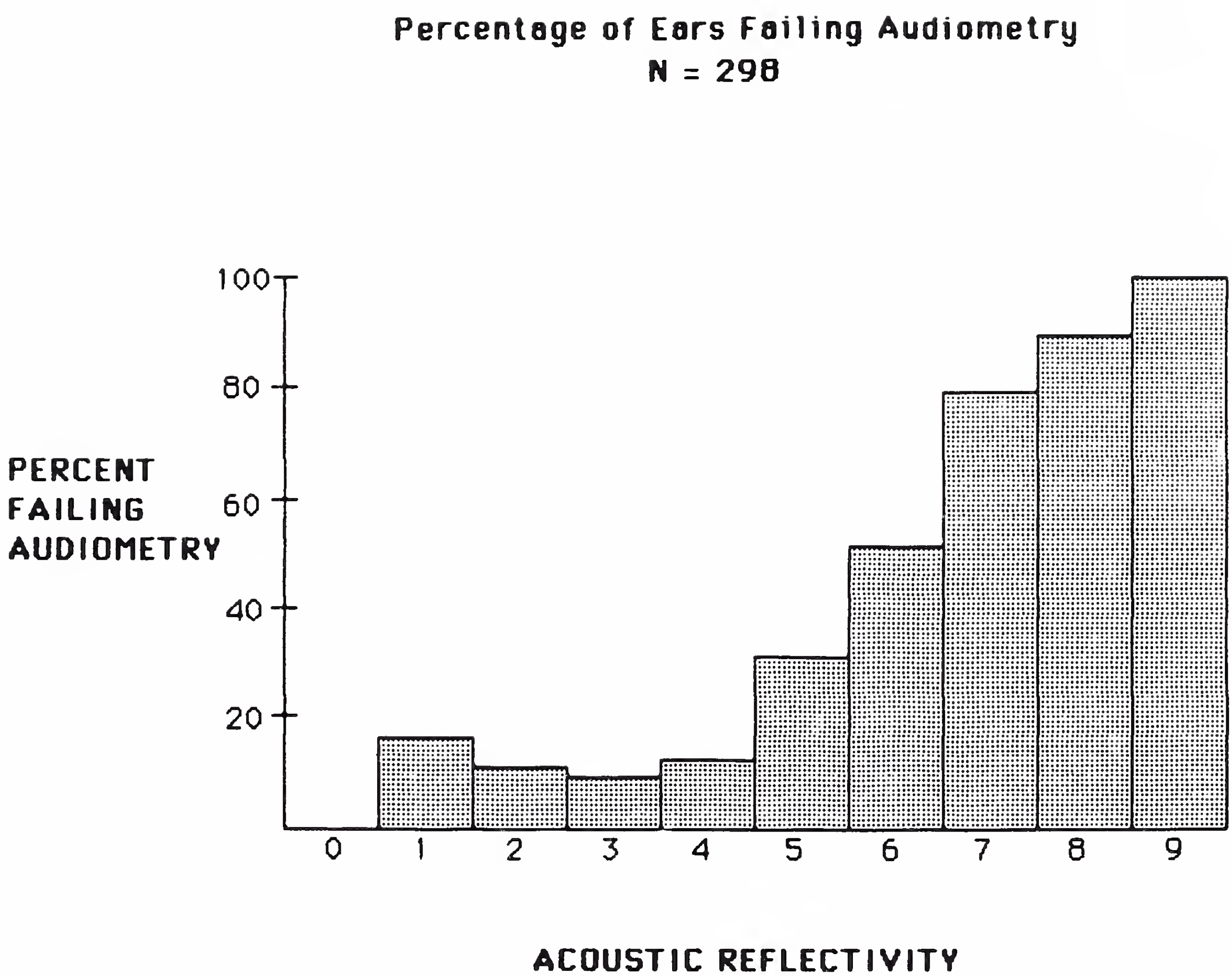

Fig. 7: The percentage of ears failing threshold audiometry, from total dataset (all ears, infected and healthy).

DATA FOR ALL EARS TESTED

N = 298

AR CUT POINT	SENSITIV.	SPECIFIC.	PPV	NPV
9.0	0.9 %	100 %	100 %	62.6 %
8.0	26.8 %	97.8 %	88.2 %	68.9 %
7.0	59.8 %	92.5 %	82.7 %	79.3 %
6.0	75.9 %	83.3 %	73.3 %	85.2 %
5.0	85.7 %	68.8 %	62.3 %	88.9 %
4.0	90.2 %	48.4 %	51.3 %	89.1 %
3.0	92.8 %	31.2 %	44.8 %	87.9 %
2.0	96.4 %	14.0 %	40.1 %	86.2 %
1.0	100 %	3.8 %	38.5 %	100 %

Table 2: Table showing indices of diagnostic efficacy of nine different cutoff values of acoustic reflectivity (AR) to predict a failed audiogram. PPV = positive predictive value, NPV = negative predictive value.

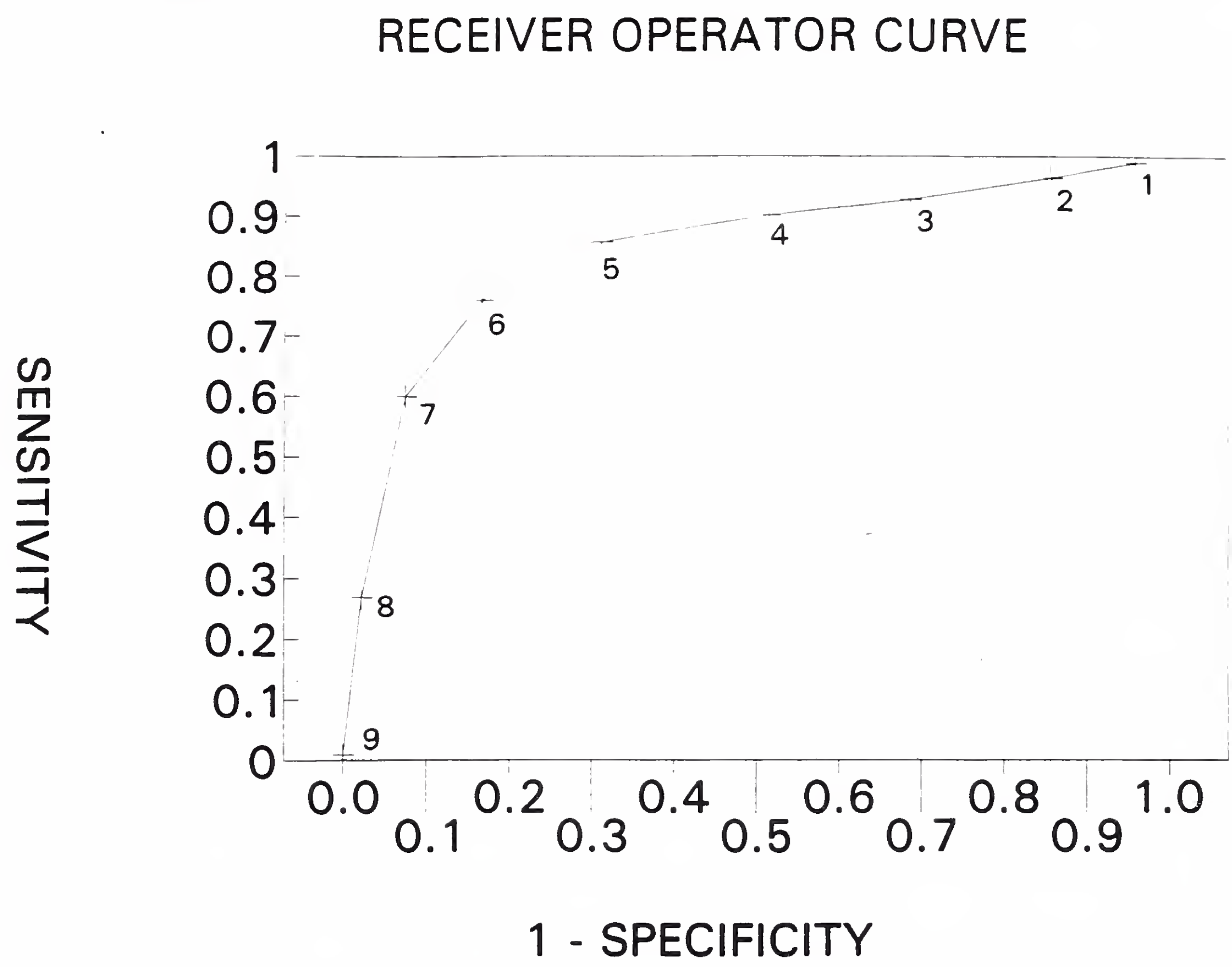

Fig. 8: Receiver operator characteristics (ROC) curve for acoustic reflectivity to predict a failed audiogram. Numbers on curve represent potential cutoff values of reflectivity.
From entire dataset (N=298).

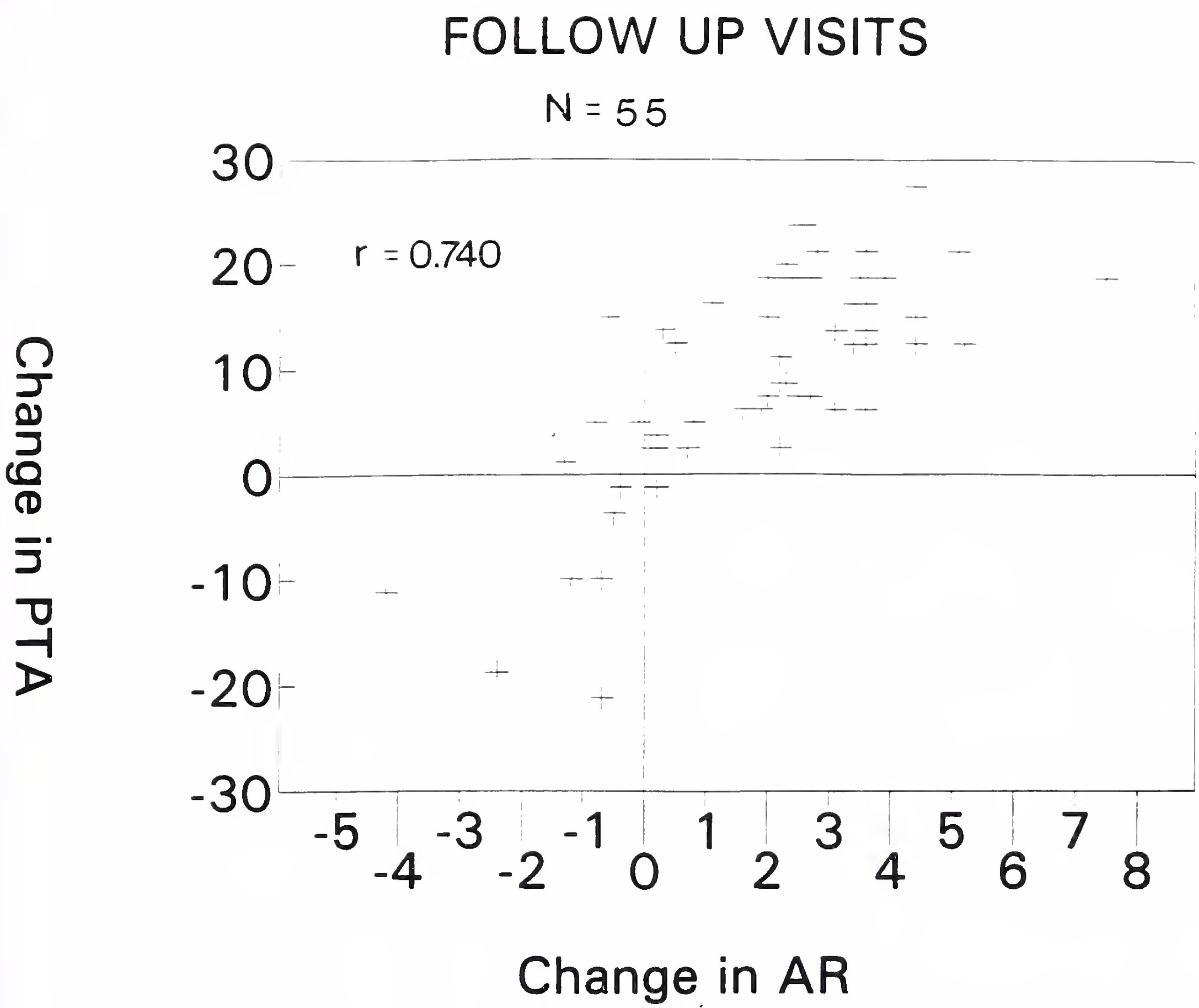

Fig. 9: Scatterplot of change in acoustic reflectivity versus change in pure tone average. For infected ears with follow up observations.

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